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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/868,196 | 08/02/2001 | Irma H. Russo | 13254-00012 | 6024 |

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| EXAMINER | |
|---|---|
| YU, MISOOK | |
| ART UNIT | PAPER NUMBER |
| 1642 | |

DATE MAILED: 12/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/868,196 | RUSSO ET AL. | |
| | Examiner | Art Unit | |
| | MISOOK YU, Ph.D. | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *09 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *45,55-65 70-78, 80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45,55-65,70-78 and 80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/09/2004 has been entered.

Claims 45, 63, 64, 73-75 are amended. Claims 45, 55-65, 70-78, and 80 are pending and examined on merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

This Office action contains new grounds of rejection.

### *Claim Rejections - 35 USC § 112, Withdrawn*

The rejection of claims 45, 55-65, 70-78, and 80 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is **withdrawn** in view of the amendment.

The rejection of claims 45, 55-65, 70-78, and 80 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is also **withdrawn** in view of the amendment.

### *Claim Rejections - 35 USC § 102, Withdrawn*

The rejection of claims 45, 55-58, 70, and 75 under 35 U.S.C. **102(b)** as being anticipated by any one of Srivastava et al (1997, IDS AX, cited in ISR, Carcinogenesis, vol. 18, pages 1799-1808), Russo et al (1990, IDS AS, J. Natl, Cancer Inst. Vol. 82, pages 1286-1287), or Russo et al (1990, IDS AT, Br. J. Cancer, vol. 62, pages 2343-7) is **withdrawn** because the amended claims are not anticipated by the art of record.

The rejection of claim 45, 70-72, and 77 under 35 U.S.C. **102(b)** as being anticipated by Saal et al, Fertil Steril. 1991 Aug;56(2):225-9 as evidenced by Russo et al (cited above, 1990, IDS AT) is **withdrawn** because the amended claims are not anticipated by the art of record.

The rejection of claim 45, and 70-77 under 35 U.S.C. **102(b)** as being anticipated by Anapliotou et al, Fertil Steril. 1996 Aug;66(2):305-11, as evidenced by Russo et al (cited above, 1990, IDS AT) is also **withdrawn** because the amended claims are not anticipated by the art of record.

***Claim Rejections - 35 USC § 103, Withdrawn***

The rejection of claim 59 under 35 U.S.C. 103(a) as being unpatentable over any one of Srivastava et al (1997, IDS AX, cited in ISR, Carcinogenesis, vol. 18, pages 1799-1808), Russo et al (1990, IDS AS, J. Natl, Cancer Inst. Vol. 82, pages 1286-1287), or Russo et al (1990, IDS AT, Br. J. Cancer, vol. 62, pages 2343-7) as applied to claims 45 and 58 above, and further in view of Silverstein et al (1994, Cancer, vol. 73, pages 1673-7, abstract only) is **withdrawn**.

The rejection of claim 65 under 35 U.S.C. 103(a) as being unpatentable over any one of Srivastava et al (1997, IDS AX, cited in ISR, Carcinogenesis, vol. 18, pages 1799-1808), Russo et al (1990, IDS AS, J. Natl, Cancer Inst. Vol. 82, pages 1286-1287), or Russo et al (1990, IDS AT, Br. J. Cancer, vol. 62, pages 2343-7) as applied to claim 45 above, and further in view of Mgbonyebi et al (1997, IDS AL) is **withdrawn**.

The rejection of claim 78 is rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Srivastava et al (1997, IDS AX, cited in ISR, Carcinogenesis, vol. 18, pages 1799-1808), Russo et al (1990, IDS AS, J. Natl, Cancer Inst. Vol. 82, pages 1286-1287), or Russo et al (1990, IDS AT, Br. J. Cancer, vol. 62, pages 2343-7) as applied to claim 45 above, and further in view of any one of Platanias et al (J Biol Chem. 1998 Mar 6;273:5577-81), Oberg et al (1989, J Natl Cancer Inst., vol. 81, pages 531-5), Recchia et al (Clin Ter. 1998 May-Jun;149:203-8), or Robinson et al (1990, Breast Cancer Res. Treat., vol. 15, pages 95-101, abstract only) is **withdrawn**.

The rejection of claim 80 under 35 U.S.C. 103(a) as being unpatentable over any one of Srivastava et al (1997, IDS AX, cited in ISR, Carcinogenesis, vol. 18, pages 1799-1808), Russo et al (1990, IDS AS, J. Natl, Cancer Inst. Vol. 82, pages 1286-1287), or Russo et al (1990, IDS AT, Br. J. Cancer, vol. 62, pages 2343-7) as applied to claim 45 above, and further in view of Sigma catalog (1995, page 263 only) is withdrawn.

***The Following Are New Grounds of Rejection***

***Claim Objections***

Claim 45 is objected to because of the following informalities: "hGC" in lines 4, and 5 of claim 45 appears to be a typographical error. Appropriate correction is required.

***Claim Rejections - 35 USC § 103***

Claims 45, 55-58, 70-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Srivastava et al (1997, IDS AX, cited in ISR, Carcinogenesis, vol. 18, pages 1799-1808), Russo et al (1990, IDS AS, J. Natl, Cancer Inst. Vol. 82, pages 1286-1287), or Russo et al (1990, IDS AT, Br. J. Cancer, vol. 62, pages 2343-7).

Claim 45 (the base claim of the claimed invention) is drawn to method of treating clinically manifest mammary tumors with an active step of administering an effective amount of hCG to a host to inhibit proliferation of mammary tumors, claim 55 further limits the tumor to be a primary tumor, claim 56 further limits the tumor to be a non-invasive carcinoma, claim 57 further limits the carcinoma to be a in situ or lobular carcinoma in situ, claim 58 further limits the tumor to be invasive carcinoma, claims 70-72 further limit the amount to be 50 to 20,000 IU per day, clams 73-75 further limit hCG to be administered every second day, 3 times per week, for several weeks following the first dose, and at least 12 weeks respectively.

Srivastava et al teach method of treating/preventing DMBA-induced mammary tumor (non invasive, invasive, carcinoma) by administering 100 IU hCG obtained from

Sigma to a host for 40 days by inhibiting proliferation of mammary cells. Note Figs. 1 and, Materials and methods at page 1800, Table I and II at page 1801. Srivastava et al teach at page 1800, left column, line 10 that the hCG is obtained from Sigma.

Russo et al (IDS AS) teach method of treating/preventing DMBA-induced mammary tumor (non invasive, invasive, carcinoma) by administering 100 IU hCG. Note Fig. 1 and 2, and Table 1.

Russo et al (IDS AT) method of treating/preventing DMBA-induced mammary tumor (non invasive, invasive, carcinoma) by administering 100 IU hCG. Note Experimental protocol at page 2343, Tables I-III.

Applicant argues that none of the cited references teaches a method of treating clinically manifest mammary tumors, i.e. tumors were not clinically manifest in the rats at the initiation of hCG treatment; Rosso et al specifically disclose that animals did not begin developing palpable tumors until six weeks after DMBA injection; and Stinvastava et al report that the earliest finding of a mammary tumor following DMBA administration was at 70 days of age. This argument has been fully considered but found unpersuasive for several reasons:

Srivastava et al., teach method of treating/preventing DMBA-induced mammary tumor (non invasive, invasive, carcinoma) by administering 100 IU hCG obtained from Sigma to a host for 40 days, and Srivastava et al., at the last sentence teach "the use of agents like hCG that induce apoptosis may constitute a useful approach for the prevention and therapy of breast cancer."

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to treat treating clinically manifest mammary tumor by administering 100 IU hCG with a reasonable expectation of success since any of the three references teach how to obtain the active ingredient, i.e. hCG that causes apoptosis of mammary cells and how to administer the active ingredient in vivo subject. With the doses in claims 70-72, and the administration schedules in claims 73-76, 100 IU for several weeks are used in all of the three references for the model animals, thus adjusting other doses for different body weight, for example, and also adjusting different schedules, for example based on progress of the treatment are well within the level of ordinary skill in the art.

Claims 45, 55-58, **60-64**, 70-76 are rejected under 35 U.S.C. **103(a)** as being unpatentable over any one of Srivastava et al (1997, IDS AX, cited in ISR, Carcinogenesis, vol. 18, pages 1799-1808), Russo et al (1990, IDS AS, J. Natl, Cancer Inst. Vol. 82, pages 1286-1287), or Russo et al (1990, IDS AT, Br. J. Cancer, vol. 62, pages 2343-7) in view of Grattarola of record (1976, Journal of the National Cancer Institute, vol. 56, pages 11-16).

See the interpretation of claims 54, 55-58, 70-76 above.

Claims 60-64 not rejected above are interpreted as drawn to method of treating metastatic mammary tumors (claim 60), clinically manifest mammary tumor in premenopausal woman (claim 61), postmenopausal woman (claim 62) with an active step of administering an effective amount of hCG to a host with at least other treatment (claim 63), said at least other treatment being surgery or chemotherapy (claim 64).

Any one of primary references teach administering hCG is useful for causing apoptosis of mammary cells and suggests that hCG might be good for breast cancer therapy.

The primary references do not specifically teach metastatic mammary tumors, clinically manifest mammary tumor in premenopausal woman, postmenopausal woman or administering hCG to a host with at least other treatment, said at least other treatment being surgery or chemotherapy.

However, Grattarola teaches method of administering 15,000 IU hCG to advanced breast cancer patients who are either pre-menopausal and post-menopausal, and had undergone surgery. Note abstract, page 11-12, Table 1. Note the amount used in the prior art is the same amount used in instant claims 70-72.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to treat teach metastatic mammary tumors, clinically manifest mammary tumor in premenopausal woman, postmenopausal woman or administering hCG to a host with at least other treatment, said at least other treatment being surgery or chemotherapy with a reasonable expectation of success since Srivastava et al., for example teach that administering hCG causes apoptosis of mammary cells, and suggest that hCG is an useful agent for breast cancer treatment, and administering hCG to metastatic mammary tumors, clinically manifest mammary tumor in premenopausal woman, postmenopausal woman or administering hCG to a host with at least other treatment, said at least other treatment being surgery or chemotherapy is taught by Grattarola.

Claim 45, 55-58, **59,** 70-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Srivastava et al (1997, IDS AX, cited in ISR, Carcinogenesis, vol. 18, pages 1799-1808), Russo et al (1990, IDS AS, J. Natl, Cancer Inst. Vol. 82, pages 1286-1287), or Russo et al (1990, IDS AT, Br. J. Cancer, vol. 62, pages 2343-7), in view of Silverstein et al., of record (1994, Cancer, vol. 73, pages 1673-7, abstract only).

See interpretation of claims 45, 55-58, 70-76 above.

Claim 59 not rejected above is interpreted as drawn to method of treating tubular or lobular mammary carcinoma by administering hCG.

Any one of the primary references teaches hCG has protective effect against breast cancer.

The primary references do not teach tubular or lobular mammary carcinoma.

However, Silverstein et al., teach that tubular or lobular invasive breast mammary carcinoma is also breast cancer and cancer staging is well known in the art. Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to select which patients has the specifically recited stage of breast cancer and administer hCG with a reasonable expectation of success.

Claims 45, 55-58, **65**, 70-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Srivastava et al (1997, IDS AX, cited in ISR, Carcinogenesis, vol. 18, pages 1799-1808), Russo et al (1990, IDS AS, J. Natl, Cancer

Inst. Vol. 82, pages 1286-1287), or Russo et al (1990, IDS AT, Br. J. Cancer, vol. 62, pages 2343-7) in view of Mgbonyebi et al (1997, IDS AL).

See interpretation of claims 45, 55-58, 70-76 above.

Claim 65 not rejected above is interpreted as drawn to method of treating clinically manifest mammary tumors by administering the active ingredient, i.e. hCG to estrogen positive mammary tumor.

Any one of the primary references teaches hCG has protective effect against breast cancer.

The primary references do not teach estrogen positive mammary tumor.

However, Mgbonyebi et al (1997, IDS AL) teach hCG is effective in inhibition of estrogen positive breast cancer cells, Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to detect which breast cancer is estrogen positive and practice instantly claimed invention with reasonable expectation of success.

Claims 45, 55-58, 70-76and **77** are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Srivastava et al (1997, IDS AX, cited in ISR, Carcinogenesis, vol. 18, pages 1799-1808), Russo et al (1990, IDS AS, J. Natl, Cancer Inst. Vol. 82, pages 1286-1287), or Russo et al (1990, IDS AT, Br. J. Cancer, vol. 62, pages 2343-7) in view of Saal et al., of record, Fertil Steril. 1991 Aug;56(2):225-9.

See interpretation of claims 45, 55-58, 70-76 above.

Claim 77 not rejected above is interpreted as drawn to method of treating clinically manifest mammary tumors by administering the active ingredient, i.e. hCG subcutaneously.

Any one of the primary references teaches hCG has protective effect against breast cancer.

The primary references do not teach injecting hCG subcutaneously.

However, Saal et al., teach administering hCG subcutaneously at page 226 under the heading "Study Protocol".

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to select subcutaneous injection method to administer hCG with a reasonable expectation of success.

Claims 45, 55-58, 70-76 and **78** are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Srivastava et al (1997, IDS AX, cited in ISR, Carcinogenesis, vol. 18, pages 1799-1808), Russo et al (1990, IDS AS, J. Natl, Cancer Inst. Vol. 82, pages 1286-1287), Russo et al (1990, IDS AT, Br. J. Cancer, vol. 62, pages 2343-7) in view of any one of Platanias et al., of record (J Biol Chem. 1998 Mar 6;273:5577-81), Oberg et al., of record (1989, J Natl Cancer Inst., vol. 81, pages 531-5), Recchia et al., of record (Clin Ter. 1998 May-Jun;149:203-8), or Robinson et al (1990, Breast Cancer Res. Treat., vol. 15, pages 95-101, abstract only)

See interpretation of claims 45, 55-58, 70-76 above.

Claim 78 not rejected above is interpreted as drawn to method of treating clinically manifest mammary tumors by administering the active ingredient, i.e. hCG in combination with Type 1 interferon.

Any one of the primary references teaches hCG has protective effect against breast cancer.

The primary references do not teach hCG treatment in combination with Type 1 interferon.

However, any one of Platanias et al of record, Oberg et al of record, or Recchia et al of record, teaches that Type I interferon has anti-tumor activity.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use Type I interferon known to have anti-tumor effect in combination with hCG with reasonable expectation of success.

Claims 45, 55-58, 70-76 and **80** are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Srivastava et al (1997, IDS AX, cited in ISR, Carcinogenesis, vol. 18, pages 1799-1808), Russo et al (1990, IDS AS, J. Natl, Cancer Inst. Vol. 82, pages 1286-1287), Russo et al (1990, IDS AT, Br. J. Cancer, vol. 62, pages 2343-7) in view of Sigma catalog of record (1995, page 263 only).

See interpretation of claims 45, 55-58, 70-76 above.

Claim 80 not rejected above is drawn to the method using recombinant hCG.

Any one of the primary references teaches hCG has protective effect against breast cancer.

The primary references do not teach hCG used is recombinant.

However, Sigma catalog says that the recombinant hCG is commercially available, therefore it is the Office's position that claim 80 is an obvious variation of the base claim and one in ordinary skill would have practiced the instantly claimed invention with reasonable expectation of success before the effective filing date of instant invention.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey C Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MISOOK YU, Ph.D.
Examiner
Art Unit 1642